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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/818,534	03/14/97	NELSON	W 3922

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EXAMINER	
HINES, J	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/818,534	Applicant(s) Nelson et al.
	Examiner Ja-Na Hines	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 7, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *2 and 9-15* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *2 and 9-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 27

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

REQUEST FOR CONTINUED EXAMINATION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 7, 2001 has been entered.

Amendment Entry

2. Amendments have been entered as filed on May 7, 2001. Claims 13-15 have been added. Claims 2 and 9-15 are pending in this office action.

Drawings

3. Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2, 9-11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 states that the sample has at least 200 fold antibodies in excess of the target antigen. It is unclear how the sample contains 200 fold excess antibodies if the antibodies were previously immobilized. Step 9(a) recites that the antibodies are immobilized on a solid phase, thus it is unclear if the antibodies in 9(c) are the same antibodies bound in step (a) or if the antibodies of (c) are different then the immobilized antibodies. Therefore, the claim is unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 9-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tarcha et al., (US Patent 5,266,498) in view of Nelson et al. (US 4,487,198). Tarcha (US Patent 5,266,498) teaches ligand binding assays for an analyte using surface-enhanced scattering signals. The prior art teaches the detection of minute quantities of a certain substance being measured in the presence of much larger quantities of other substances (col. 1 lines 55-58). This is possible because of the high affinity a binding molecule can have for a ligand wherein the result is a high

degree if specificity, the most common ligand binding assays are immunoassays using antibodies (col. 1-2 lines 58-49). Tarcha et al., teaches direct immunoassays, radioimmunoassays and enzyme immunoassays. The use of Raman light scattering as a means of detecting or measuring the presence of a labeled specific binding member avoids previous drawbacks in the art (col 3 lines 15-20). Raman techniques are considered to have the potential to be useful as an analytical tool to identify certain molecules, and as a means of studying molecular structure, however other useful tools include infrared spectroscopy (col. 4 lines 5-10). Resonance Raman scattering shows the electronic vibrational absorption to be 1000 times more efficient (col. 4 lines 23-26) and there was a significant increase when molecules are brought into close proximity to certain metal surfaces, i.e., surface enhanced raman scattering (SERS) (col. 4 lines 34-44). The SERS effect can be enhanced through combination with the resonance raman effect to result in an enhancement in the intensity of the raman scattering of seven orders of magnitude or more (col. 5 lines 16-25). SERS was then applied to immunoassays, which has several unique advantages because only those reporter molecules which have become immobilized on the SERS- active surface will contribute a significant signal and molecules bound in different environments or different orientations can exhibit differences in their raman scattering characteristics (col. 5 lines 35-50). Tarcha et al., teaches the attachment of specific binding members, i.e., antibodies to the SERS-active surface (col. 8 lines 45-55). Example 6 teaches dye-antibody conjugates and raman readout in a sandwich immunoassay, while example 7 teaches a no wash immunoassay. However, Tacha et al., does not teach the using the laser light at 242-257nm.

Nelson et al. (US 4,487,198), teaches an apparatus and a method of detection and identification of bacteria by means of ultra-violet excited resonance Raman spectra. The method uses the emitted light energy, which is resonance enhanced Raman scattering and is measured as backscattered energy where the energy processed produces spectra which are characteristic of the bacteria (abstract). The method comprises exciting taxonomic markers in a bacterium with ultra violet light as a lower resonance enhanced Raman back scattered energy; converting the energy to correspond to the taxonomic markers; and displaying the spectra such that the bacterium may be detected and identified (col. 6 lines 43-56). Nelson et al., teaches an effective range of use being 190-260nm (col. 5 lines 10-15), and further showed five different types of bacteria being excited at 242 nm (col. 5 lines 21-22). The resonance Raman spectra exhibits differences in the composition in the organism, nucleic acids, proteins and other markers are major contributors to the spectra reported (col. 5 lines 22-27). Also rapid analysis is possible, Nelson et al., anticipates a library of spectra will be obtained and can then be rapidly scanned by a computer on the basis of resonance Raman spectra (col 5-6 lines 64-2). The test samples were suspensions of bacterial cultures and other microorganisms can be embodied in any biologically acceptable carrier or medium (col. 6 lines 35-40). However, Nelson et al., does not teach the immobilization of antibodies to a solid phase.

Therefore, it would have been have been obvious at the time of applicants' invention to have used capture molecules like antibodies immobilized to a solid phase which specifically bind in antibody-antigen complex as taught by Tarcha et al., in conjunction with a method for detecting

the presence of a specific microorganism in a sample as taught by Nelson et al., because Nelson et al., teaches an effective range of use being 190-260nm and further showed five different types of bacteria being excited at 242 nm.

6. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tacha et al., (US Patent 5,266,498) in view of Nelson et al. (US 4,487,198) in further view of Muller (US Patent 5,126,244). Tarcha et al., (US Patent 5,266,498) and Nelson et al. (US 4,487,198) have been discussed above, however neither specifically teaches the use of *E.coli* and *E. coli* antibodies. Muller (US Patent 5,126,244) teaches the determination of antigens. Antigens from bacteria for immunological can be found (col. 1 lines 35-40). Example 1 A.3 teaches the qualitative determination of *E. coli* antigens with *E. coli* antibodies used in an enzyme immunoassay.

Therefore, it would have been have been obvious at the time of applicants' invention to have used antibodies to *E.coli* as taught by Muller in the method and system as taught by Tarcha et al., in view of Nelson et al., wherein Nelson et al., already teaches the detection of bacteria however, Muller teaches the specific detection of *E.coli* using *E. coli* antibodies in an immunoassay.

7. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) in view of Herron et al., in further view of Muller (US Patent 5,126,244).

Nelson et al. (US 4,487,198) Herron et al., and Muller have been discussed, however neither specifically teaches the use of *E.coli* and *E. coli* antibodies.

Therefore, it would have been have been obvious at the time of applicants' invention to have used antibodies to *E.coli* as taught by Muller in the method and system as taught by Nelson et al., in view of Herron et al., wherein Nelson et al., already teaches the detection of bacteria however, Muller teaches the specific detection of *E.coli* using *E. coli* antibodies in an immunoassay.

8. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chadha et al., in view of Herron et al., in further view of Muller (US Patent 5,126,244). Chadha et al. (US 4,487,198) Herron et al., and Muller have been discussed, however neither specifically teaches the use of *E.coli* and *E. coli* antibodies.

Therefore, it would have been have been obvious at the time of applicants' invention to have used antibodies to *E.coli* as taught by Muller in the method and system as taught by Nelson et al., in view of Herron et al., wherein Chadha et al., already teaches the detection of bacteria however, Muller teaches the specific detection of *E.coli* using *E. coli* antibodies in an immunoassay.

Response to Arguments

9. Applicant's arguments filed November 20, 2000 have been fully considered but they are not persuasive.

10. Claims 2, 9-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) in view of Herron et al., is maintained.

Applicants purports that unexpected results have been achieved, because the sample has at least 200 fold antibodies in excess of the target antigen as cited in claim 9 only. However, Herron et al., (US Patent 5,512,492) that the biosensor system has capture molecules site-specifically immobilized such that the percentage if capture sites available is 50 to 75% or more of the number of immobilized capture molecules (col. 3 lines 40-44). Table II shows a summary of solid phase immunoassays. These results show increased sensitivity when detecting target antigens. Therefore, Nelson et al., in view of Herron et al., teaches the use of excess antibodies for more sensitive detection.

Claims 12 and 14 do not include the 200 fold antibody limitation, therefore the rejection is maintained, because the system of claims 12, and 14 do not have a means has displaying any unexpected results. In this case, applicants use of antibodies is for the same purpose, i.e., immobilization and achieves the same results, Raman spectra analysis, as the prior art references, therefore no unexpected results have been established. No more then routine skill have been required at the time of applicants' invention to have used capture molecules like antibodies immobilized to a solid phase which specifically bind in antibody-antigen complex where the

antigen or analyte is a microorganism as taught by Herron et al., in conjunction with a method for detecting the presence of a specific microorganism in a sample without interference to the energy spectra as taught by Nelson et al., because Herron et al., teaches immobilizing bacteria using antibodies is well known in the art as a method of immobilization.

11. Claims 2, 9-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chadha et al., in view of Herron et al., is maintained. In this case, Herron et al., has been discussed above, and teaches the use of immobilized antibodies in excess of the target antigen. Herron et al., teaches increased sensitivity. Accordingly there would have been a reasonable expectation of success for one skilled in the art to modify the method and system of Chadha et al., by substituting the immobilization of antibody to a solid phase because the specificity of antibodies are conventionally used to bind and immobilize bacterial antigens for an assay as taught by Herron et al., to increase sensitivity without obscuring the Raman spectra energy, thus the results are expected.

12. Applicants submitted a declaration of Chris Brown, Ph.D. This declaration purportedly teaches that the practice of the claimed method as set forth in claim 9 and 12 yields unexpectedly significant results, wherein a microorganism can be detected in a sample wherein the ratio of antibody to microorganism in the sample is $10^6/1$ as evidenced by the spectral results set forth in exhibit A on page 14. The declaration under 37 CFR 1.132 filed May 7, 2001 is insufficient to

overcome the rejection of claims 2, 9 and 12-15 because the Declaration does not teach specifically the 200 fold antibody discussed in claim 9. The declaration states a different ratio. Claim 12 does not require the use of the antibody at that level, therefore no unexpected results can be associated with the system. Furthermore, exhibit A appears to be a scientific paper, but it lacks a date. Therefore it is impossible to assess whether the paper has the appropriate priority. The claims are drawn to a specific ratio, 200 fold and not $10^6/1$ as specifically recited in the declaration, therefore the statement that unexpected results have been achieved is not commensurate with the scope of the claims.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

July 9, 2001

7/9/01

JENNIFER E. GRASER
PRIMARY EXAMINER